

Amendments to the Claims

1. (original) A modified nucleoside analogue having the formula (I):

P-S-B-L-R

where:

P is a 5' triphosphate or analogue or derivative thereof;

S is a substituted or unsubstituted five- or six-membered sugar, sugar analogue or acyclo sugar analogue, but excluding a dideoxy-sugar;

B is a substituted or unsubstituted nitrogenous base or base analogue or derivative thereof;

L is a linker group; and

R is a substituted or unsubstituted metallocene moiety or substituted or unsubstituted metal complex or substituted or unsubstituted redox-active organic moiety.

2. (currently amended) A The modified nucleoside analogue as claimed in claim 1 wherein P is an enzyme-compatible triphosphate moiety.

3. (currently amended) A The modified nucleoside analogue as claimed in claim 2 wherein P is selected from the group consisting of triphosphate, α -thiotriphosphate, β -thiotriphosphate, γ -thiotriphosphate, α -dithiotriphosphate, or β,γ -methylenetriphosphate.

4. (currently amended) A The modified nucleoside analogue as claimed in ~~any one of claims 1 to 3~~ claim 1 wherein group S is substituted or unsubstituted ribose, 2'-deoxyribose, 3'-fluoro-2'-deoxyribose 3'-amino-2'-deoxyribose, a bicyclic "locked" LNA sugar selected from 2'-O,4'-C-methylene-, 2'-C,4'-C-ethylene- or 2'-O,4'C-ethylene-bridged furanose, or an acyclo moiety comprising a 2-hydroxyethoxymethyl group or analogue thereof.

5. (currently amended) A The modified nucleoside analogue as claimed in claim 4 wherein group S is substituted with substitutes selected from one or more of fluoro, amino, hydroxyl, methyl or methoxy groups.

6. (currently amended) A The modified nucleoside analogue as claimed in claim 4 wherein group S is unsubstituted.

7. (currently amended) A The modified nucleoside analogue as claimed in ~~any one of the preceding claims~~ claim 1 wherein ~~group~~ B is a substituted or unsubstituted. purine or pyrimidine or other nucleobase or nucleobase analogue.

8. (currently amended) A The modified nucleoside analogue as claimed in claim 7 wherein B is adenine, guanine, cytosine, uracil, or thymine, inosine or a derivative of an adenine, guanine, cytosine, uracil, thymine or inosine.

9. (currently amended) A The modified nucleoside analogue as claimed in claim 8 wherein B is a 7-deaza variant of adenine or guanine.

10. (currently amended) A The modified nucleoside analogue as claimed in claim 8 wherein said derivative includes at least one this group.

11. (currently amended) A The modified nucleoside analogue as claimed in ~~any one of the preceding claims~~ claim 1 wherein L is or contains a saturated or unsaturated aliphatic chain, with or without cyclic groups or an amine or a carboxyl or an amide.

12. (currently amended) A The modified nucleoside analogue as claimed in claim 11 wherein L is substituted with fluoro, ether or hydroxy substituents.

13. (currently amended) A The modified nucleoside analogue as claimed in claim 11 ~~or claim 12~~ wherein L is of 1-24 bonds in contour length.

14. (currently amended) A The modified nucleoside analogue as claimed in claim 13 wherein L is of 3-12 bonds in length.

15. (currently amended) A The modified nucleoside analogue as claimed in claim 11 wherein L is selected from propenyl or propargyl derivatives.

16. (currently amended) A The modified nucleoside analogue as claimed in ~~any one of the preceding claims~~ in claim 1 wherein R is a substituted or unsubstituted metallocene, a substituted or unsubstituted metal complex or an organic redox moiety and wherein substituents

are selected from one or more of the groups fluoro, bromo, chloro, methyl, ethyl, hydroxy, hydroxymethyl, hydroxyethyl, methoxy, ethoxy, acetyl, cyano, thiocyno, amino, nitro, vinyl, amido, methylamido, and dimethylamido.

17. (currently amended) A The modified nucleoside analogue as claimed in claim 16 wherein R is a metallocene having a redox potential in the range of -1.0 to +1.0 V vs. Standard Hydrogen Electrode (SHE).

18. (currently amended) A The modified nucleoside analogue as claimed in ~~claim 16 or claim 17~~ claim 1 wherein R is ferrocene.

19. (currently amended) A The modified nucleoside analogues as claimed in claim ~~16~~ 1 wherein R is a quinone or quinone-containing moiety.

20. (currently amended) A The modified nucleoside analogue as claimed in claim 19 wherein said quinone or quinone-containing moiety is selected from anthraquinones and substituted anthraquinones.

21. (currently amended) A The modified nucleoside analogue as claimed in claim 16 wherein R is a metal complex exhibiting reversible electron transfer with E_0 in the range -1 V to +1 V vs standard hydrogen electrode (SHE).

22. (currently amended) A The modified nucleoside analogue as claimed in claim ~~8~~ 1 wherein B is selected from substituted or unsubstituted cytosine, uracil or thymine and L is joined to the C5 carbon of the cytosine, uracil or thymine.

23. (currently amended) A The modified nucleoside analogue as claimed in claim ~~8~~ 1 wherein B is selected from substituted or unsubstituted adenine or guanine or a 7-deaza-derivative of adenine or guanine in which the N7 is replaced by a C7 and L is joined to the C8 carbon or to the C7 carbon.

24. (currently amended) A method of synthesising a the modified nucleoside analogue ~~according to any one of claims 1 to 23~~ of claim 1 comprising reacting a nucleoside or nucleotide precursor with a metallocene, metal complex or organic redox moiety precursor so as to form a

link between the nucleos(t)ide analogue and the metallocene, metal complex or organic redox moiety.

25. (currently amended) A method as claimed in claim 24 further comprising the step of subsequently incorporating a 5' triphosphate or derivative thereof if wherein the starting nucleoside for nucleotide precursor does not include such a triphosphate or triphosphate derivative.

26. (currently amended) A method as claimed in claim 25 ~~or claim 25~~ wherein the link between the nucleos(t)ide precursor and the metallocene, metal complex or organic redox moiety is formed by a condensation reaction and the method further includes the step of adding a condensing agent.

27. (currently amended) A method as claimed in claim 24 ~~or claim 25~~ wherein the link between the nucleos(t)ide analogue and the metallocene, metal chelate or organic redox moiety is formed by a displacement reaction.

28. (currently amended) A method as claimed in ~~any one of claims 24 to 26~~ claim 24 wherein the method comprises reacting a nucleoside or nucleotide precursor with a metallocene precursor in the presence of a condensing agent so as to form a link between the nucleoside analogue and the metallocene or derivative thereof.

29. (currently amended) A method as claimed in ~~any one of claims 24 to 26~~ claim 24 wherein the nucleotide precursor is selected from uridine 5'-triphosphate, cytidine 5'-triphosphate, adenosine 5'-triphosphate, guanosine 5'-triphosphate, 2' deoxyadenosine 5'-triphosphate, 2'-deoxyguanosine 5'-triphosphate, 2' deoxythymidine 5'-triphosphate, 2'-deoxyuridine 5'-triphosphate, 2' deoxycytidine 5'-triphosphate, 5-aminoallyl-uridine-5'-triphosphate, 5-aminopropargyl-uridine-5'-triphosphate, 5'-aminoallyl-cytidine-5'-triphosphate, 5-aminopropargyl-cytidine-5'-triphosphate, 7-aminopropargyl-deazaadenosine-5'-triphosphate, 7-aminopropargyl-deazaguanosine-5'-triphosphate, 5-aminoallyl-2'-deoxyuridine-5'-triphosphate, 5-aminopropargyl-2'-deoxyuridine-5'-triphosphate, 5-aminoallyl-2'-deoxycytidine-5'-triphosphate, 5-aminopropargyl-2'-deoxycytidine-5'-triphosphate, 7-aminopropargyl-7-deaza-2'-deoxyadenosine-5'-triphosphate, 7-aminopropargyl-7-deaza-2'-deoxyguanosine-5'-

triphosphate, 5-aminopropargyl-acyclouridine-triphosphate, 5-aminopropargyl-acyclocytidine-triphosphate, 7-aminopropargyl-acyclodeazaadenosine-triphosphate, or 7-aminopropargyl-acyclodeazaguanosine-triphosphate.

30. (currently amended) A method as claimed in ~~any one of claims 24 to 29~~ claim 24 wherein the metallocene precursor is a carboxylic acid.

31. (original) A method as claimed in claim 30 wherein the metallocene precursor is ferrocenecarboxylic acid or ferroceneacetic acid or derivative thereof.

32. (original) A method as claimed in claim 26 wherein the condensing agent is selected from any one of a carbodiimide, for example dicyclohexylcarbodiimide, uronium compounds, activated ethers and other compounds employed in the formation of amide bonds.

33. (currently amended) A method as claimed in claim ~~31-26~~ wherein the condensing agent is 0-benzotriazol-1-yl-N,N,N',N'-tetramethyluronium hexafluorophosphate (HBTU).

34. (currently amended) An oligo- or poly-nucleotide probe, primer or enzymatic reaction product comprising at least one residue of a nucleoside analogue according to ~~any one of claims 1 to 23~~ claim 1.

35. (currently amended) An oligo- or poly-nucleotide probe, primer or enzymatic reaction product as claimed in claim 34 wherein the at least one residue of a the nucleoside analogue comprises at least one residue of a metallocene nucleoside analogue ~~according to any one of claims 1 to 23~~.

36. (currently amended) A method of nucleotide chain incorporation, the method comprising reacting a template nucleotide chain with a modified nucleoside analogue ~~according to any one of claims 1 to 23~~ of claim 1 in the presence of a processive nucleotidyl transferase or polymerase.

37. (currently amended) A method of nucleotide chain extension, the method comprising reacting a nucleotide chain with a modified nucleoside analogue ~~according to any one of claims 1 to 23~~ of claim 1 in the presence of a non-processive nucleotidyl transferase such a terminal transferase or poly(A) polymerase.

38. (currently amended) A method of electrochemical detection of DNA, RNA, DNA/RNA chimers or nucleic acid analogues, the method comprising incorporating a the modified nucleoside analogue ~~according to any one of claims 1 to 23 of claim 1~~ into a nucleic acid chain and detecting the analogue on the basis of its redox potential.

39. (currently amended) A method of electrochemical detection of DNA, RNA, DNA/RNA chimers or nucleic acid analogues, the method comprising incorporating two or more different modified nucleoside analogues ~~according to any one of claims 1 to 23 of claim 1~~ into the same or different nucleic acid chains, and detecting the modified nucleoside analogues on the basis of their different redox potentials.

40. (currently amended) A kit comprising ~~at least one redox-labelled nucleotide(s) as claims in any one of claims 1 to 23~~, and the analogues of claim 1 and at least one nucleotidyl transferase enzyme(s).

41. (original) A kit as claimed in claim 40 further comprising one or more of an appropriate unlabelled nucleotide mix, an optimised reaction buffer, control template and primer so that the user may determine the efficiency of DNA synthesis.

42. (currently amended) A The modified nucleoside analogue as claimed in claim 21 said metal complex is selected from chelates and cryptates of transition metals including iron, copper, cobalt, ruthenium, rhodium, osmium complexed with bi-, tri-, tetra-, hexa- or octadentate ligands, said metal complex.

43. (currently amended) A The modified nucleoside as claimed in claim 42 wherein said metal complex include one or more ligands selected from tridentate N-donor ligands, such as terpyridine (terpy), bis(benzimidazolyl)pyridines (bzimpy) and bis(pyrazolyl)pyridines (bpp), as well as mixed O,N,O donor ligands such as pyridinedicarboxylic acid (dipic).